Armed Forces College of Medicine

AFCM

Neuro-Muscular Blockers

Recorded by

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1- Differentiate between competitive and depolarizing Neuro-Muscular blockers regarding mechanism of actions and adverse effects.

2- Identify the reversal of Neuro-Muscular blockers.

Introduction

The neuromuscular junction:

Skeletal muscles are supplied by somatic nerves.

The region of contact between muscles and nerve is called motor end plate.

In the motor end plate there are nicotinic receptors and the transmitter is acetylcholine. Acetylcholine released is hydrolyzed by true cholinesterase.

Classification of skeletal muscle relaxants

1. Drugs which depress acetylcholine at nerve terminal

a. Inhibition of acetylcholine synthesis:

i. Hemicholinium

ii. Triethylcholine

b. Inhibition of acetyl choline release:

i. Excess Mg++, lack of Ca++

ii. Local anesthetic e.g. procaine

iii. Botulinum toxin

c. Inhibition of acetylcholine storage: vesamicol

Classification of skeletal muscle relaxants

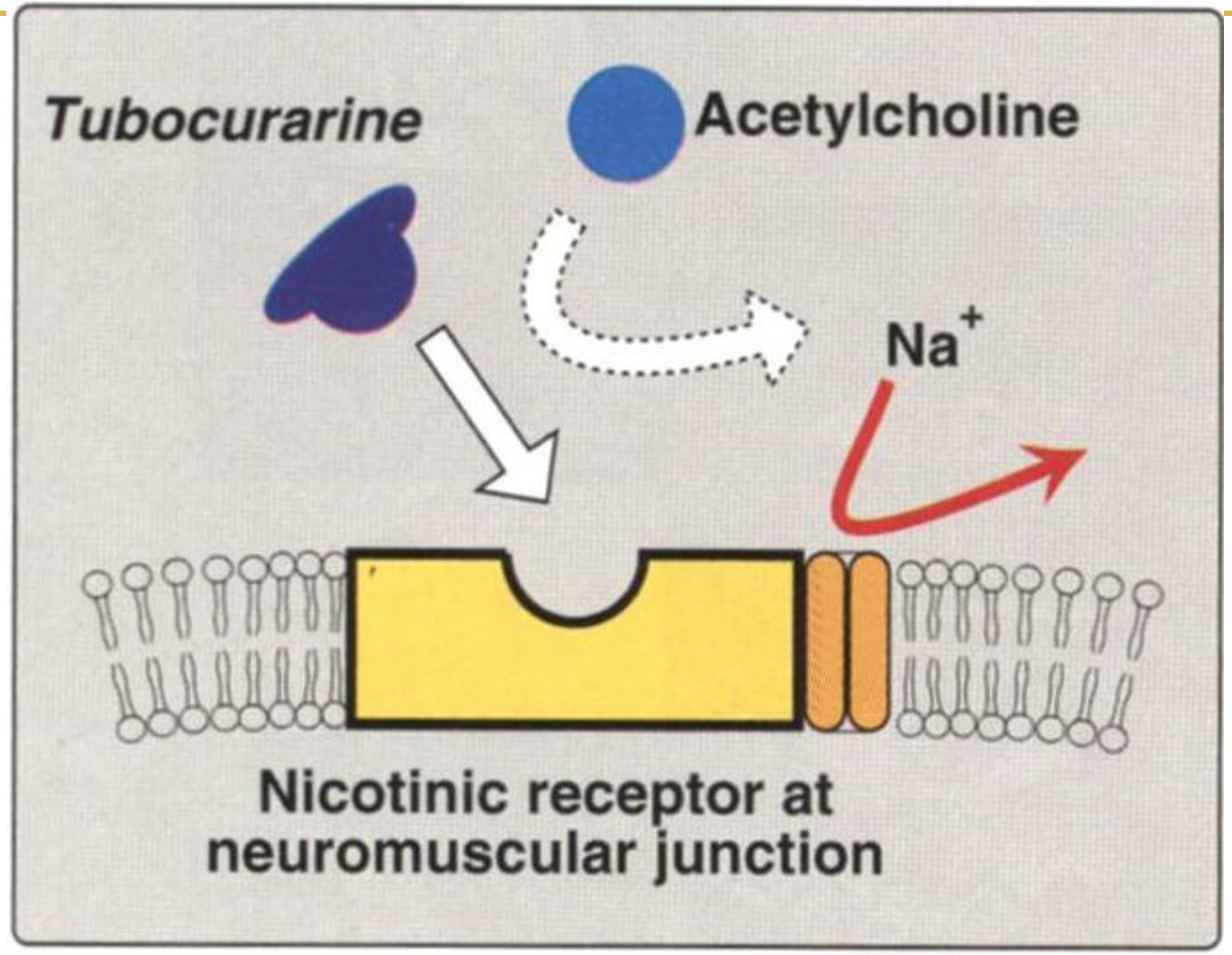
2. Neuromuscular blockers:

a. Competitive (non-depolarizing):

They compete with acetylcholine for nicotinic receptors at motor end plate → transmission failure → muscle paralysis e.g.

- Tubo-curarine
- Gallamine
- Pancuronium
- Vecuronium
- Mivacurium
- Atracurium

Mechanism of action of Neuromuscular Blockers



Classification of skeletal muscle relaxants

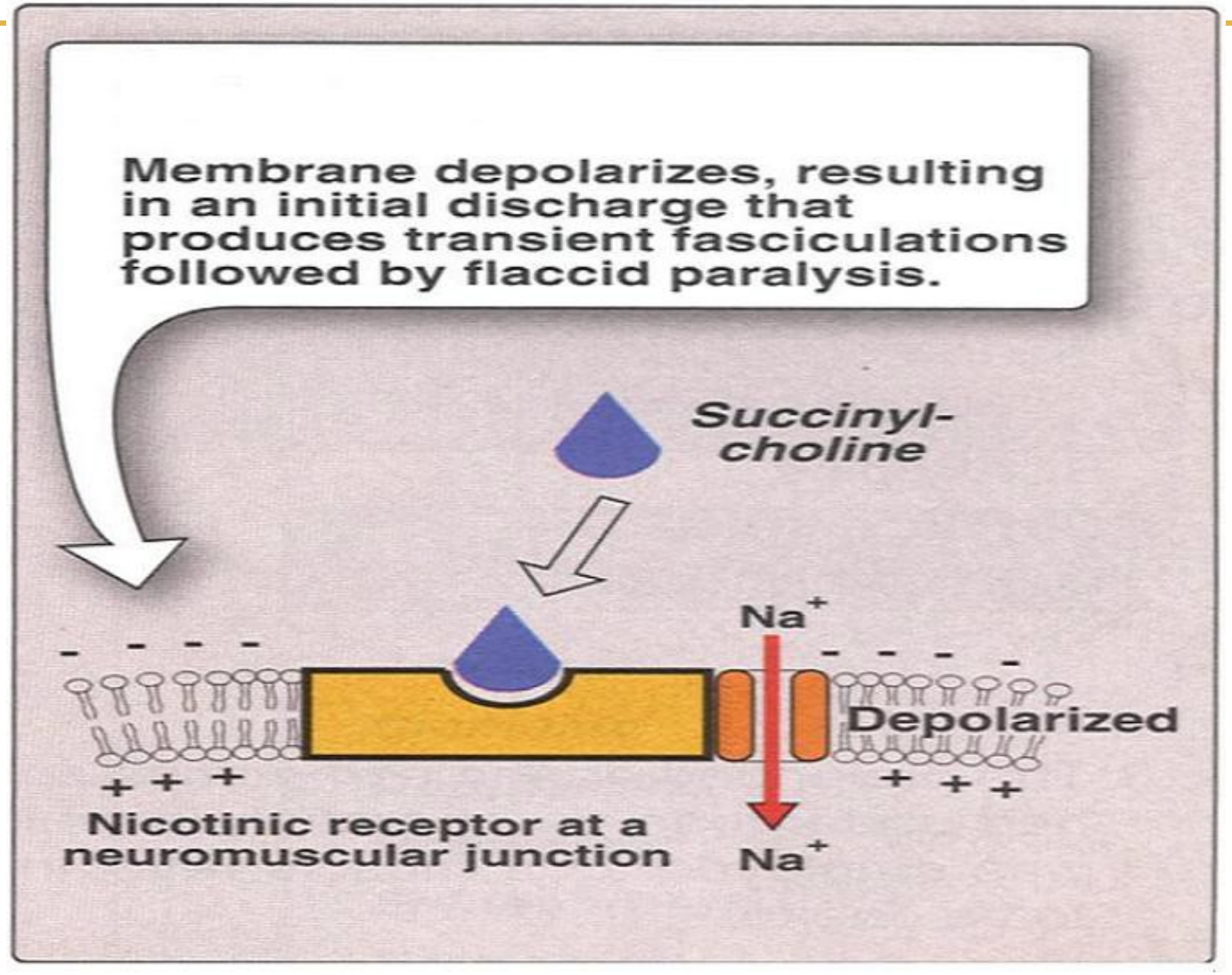
2. Neuromuscular blockers:

b. Depolarizing: e.g. succinylcholine

They produce prolonged depolarization at the motor end plate → transmission failure.

They produce initial stimulation of muscle (fasciculations) followed by paralysis.

Mechanism of action of Neuromuscular Blockers



Neuro-Musclular Blockers

I. Competitive *(Non-Deploarizing)* Blockers:

1- Tubocurarine

- **Pharmacokinetics:**

-Quaternary ammonium compound, not absorbed orally and do not pass B.B.B.

-It‟s given parenterally.

-It is mainly metabolized in liver and ⅓ is excreted unchanged in urine.

I. Competitive (Non-Deploarizing) Blockers

- **Pharmacological actions:**

1. Curare competes with acetylcholine at the nicotinic receptors in the motor end plate → muscle paralysis in the following order: muscles of the face and fingers, limbs, neck and trunk, intercostals and lastly diaphragm which may cause death due to respiratory failure.
Recovery occurs in the reverse order after ½ - 1 hour.
2. Weak ganglion blocking action
3. Histamine release →bronchospasm and

Toxicity

➢ Toxicity:

- Respiratory failure
- Histamine release
- Hypotension
- Bronchospasm

➢ Treatment of toxicity:

- ❑ Artificial respiration under +ve pressure
- ❑ Antidote: neostigmine I.V. preceded by atropine to antagonize muscarinic effects of neostigmine
- ❑ Antihistaminics

Synergists and antagonists

➢ Synergists:

- Inhalation anesthetics e.g. enfluane, isoflurane
- Streptomycin, neomycin
- Hypokalemia, acidosis
- Chlorpromazine

➢ Antagonists:

o Anticholinesterases e.g. neostigmine and edrophonium

2- Gallamine (Flaxedil)

Synthetic curare substitute (1/5 activity)

- Shorter duration
- Weak ganglion blocking action
- Weak histamine release
- ↑ Heart rate (atropine-like action)

3- Pancuronium

- **5 times more potent than curare**

- No histamine release
- No ganglion blocking effect
- Moderate ↑ heart rate

4- Vecuronium

- Short duration of action
- No effect on heart rate

5- Atracurium

- Rapidly degraded in physiological pH
- Does not depend on kidney or liver function for elimination.
- Thus may be used in renal and hepatic insufficiency

6- Mivacurium

- More potent than curare

- Shorter duration of action (10-20 min)
- No ganglion blocking action
- Weak histamine release

II. Depolarizing Neuro-Muscular Blockers

•Succinylcholine

➢ Pharmacokinetics:

- Given I.V. with short duration of action (5 min).

Due to rapid hydrolysis by pseudocholinesterase enzyme in liver and plasma.

II. Depolarizing Neuro-Muscular Blockers

•Succinylcholine

➢ Pharmacological actions:

- It produces depolarization not followed by repolarization.
- Relaxation is preceded by muscle fasciculations and it is not antagonized by neostigmine or edrophonium
- Ganglion stimulant effect
- Histamine release

Adverse Effects of Succinylcholine

1. Succinylcholine apnea:

Due to lack of plasma cholinesterase which may be due to genetic abnormality or liver disease or organophosphorus poisoning

2. Hyperkalemia:

Significant in patients with burns or massive trauma

3. ↑I.O.P.:

Avoided in eye injuries

4. Post-operative muscle pain

5. Malignant hyperthermia:

Treated with dantrolene I.V.

6. Respiratory failure:

Treated with artificial respiration and fresh blood transfusion (contain pseudo-cholinesterase).

Competitive and depolarizing N-M blockers:

Depolarizing	Competitive	
Succinylcholine	Curare	Example:
Maintained depolarization	Competes with A.Ch for Nm-R	:Mechanism
Partial agonist	Antagonist	Nature:
Reversible non-competitive	Reversible Competitive	Block:
Paralysis →Twitches	Paralysis without twitches	Effect:
Potentiated	Antagonize	Neostigmine :

Therapeutic uses of neuro-muscular blockers

1- Adjuvants in general anesthesia

2- Facilitate endotracheal intubation and endoscopies

3- In electroshock therapy

4- Convulsive states e.g. tetanus

5- Botulinum toxin (Botox) → relaxes facial wrinkles

Summary of Skeletal Muscle Relaxant

Classification of skeletal muscle relaxants:

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Summary of Skeletal Muscle Relaxant

Classification of skeletal muscle relaxants:

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Lecture Quiz

1)- All of the folowing are adverse effects of suucinylcholine EXCEPT:

a- Hypokalemia
b- Apnea
c- ↑I.O.P
d- Malignant hyperthermia

a- Hypokalemia

Lecture Quiz

2)- The folowing drug is a competitive N-M blocker 5 times more potent than curare:

a- Pancuronium
b- Gallamine
c- Mivacurium
d- Atracurium

a- Pancuronium

Lecture Quiz

3)- All of the folowing drugs are competitive N-M blockers EXCEPT:

a- Pancuronium
b- Gallamine
c- Mivacurium
d- Succinylcholine

d- Succinylcholine

SUGGESTED TEXTBOOKS

1- Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer

2- Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.

THANK YOU